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14. ABSTRACT
This randomized, clinical trial was designed to extend recruitment to an additional active duty site (Womack Army Medical Center at Ft Bragg) in support of a previously funded clinical trial to evaluate the efficacy of virtual reality exposure therapy (VRET) and prolonged exposure therapy (PE) with a waitlist (WL) group in the treatment of posttraumatic stress disorder (PTSD) in active duty (AD) Soldiers with combat-related trauma. Soldiers with PTSD from deployments to Iraq or Afghanistan were randomized to 10 sessions of either PE or VRE or were assigned to a minimal attention wait list. All assessments were conducted by a psychologist blind to treatment group. External, independent treatment fidelity reviews were conducted for both treatments. Service members were assessed before randomization, after 5 sessions, at posttreatment, and 3- and 6-months posttreatment. PTSD was assessed with the Clinician Administered PTSD Scale (CAPS). Difficulties with personnel, a slow pace of recruitment, and ultimately the analysis of the data from the original study site called into question the value of continuing this effort, which resulted in the study ending with 23 subjects randomized.

15. SUBJECT TERMS
exposure therapy, posttraumatic stress disorder, virtual reality, military, prolonged exposure

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INTRODUCTION:

This study was designed to extend recruitment to an additional active duty site (Womack Army Medical Center at Fort Bragg) in support of a previously funded randomized clinical trial to evaluate the comparative efficacy of virtual reality exposure therapy (VRET) and prolonged exposure therapy (PE) with a waitlist group (WL) for the treatment of active duty Soldiers with combat-related posttraumatic stress disorder (PTSD). The study was designed to test the general hypotheses that 10 sessions of VRET would successfully treat PTSD, therapeutically affect levels of physiological arousal, and significantly reduce perceptions of stigma toward seeking behavioral health services. Soldiers returning from deployments to Iraq or Afghanistan who were diagnosed with combat-related PTSD following administration of the Clinician-Administered PTSD Scale (CAPS) were randomized to one of three groups: 1) PE; 2) VRET; or 3) WL. Soldiers underwent clinical assessments at baseline and after 5 and 10 treatment sessions. Outcome measures were also collected at 12 and 26 weeks post-treatment. Physiological arousal, patient satisfaction with treatment, and stigma toward seeking behavioral health services were also explored.

KEYWORDS.

Virtual Reality Exposure Therapy (VRET)
Prolonged Exposure Therapy (PE)
Post-Traumatic Stress Disorder (PTSD)
Clinician-Administered PTSD Scale (CAPS)

BODY:

Overview

This study was a randomized, waitlist-controlled clinical trial in which post-Iraq, post-Afghanistan deployed Soldiers with deployment-related PTSD were randomized to one of three groups: 1) PE (n = 8), 2) VRET (n = 8), or 3) Waitlist (WL; n = 7). Note that numbers in each treatment group represent only those randomized under the Womack Army Medical Center site funded by this project.

The objectives/hypotheses of the VRET/PE study were as follows:

1. We will test the hypothesis that 10 sessions of VRET and PE will reduce PTSD symptoms compared to the waitlist.
2. We predict that 10 sessions of VRET will significantly reduce PTSD symptoms relative to PE and Waitlist assignment.
3. We will examine physiological responses during treatment to test the hypothesis that VRET will result in heightened in-session physiological responses compared to PE. In addition, we predict that VRET will result in greater reductions in physiological responses after 10 treatment sessions compared to PE.
4. We will determine whether Soldiers report reduced fears of treatment stigma following VRET compared to PE.
5. We predict that Soldiers completing 10 sessions of VRET will have higher levels of treatment adherence (lower dropout rates) and ratings of treatment satisfaction than Soldiers completing 10 sessions of PE.

Participants

All participants were diagnosed with current PTSD as assessed by the Clinician-Administered PTSD Scale (CAPS). The diagnosis of PTSD was made by a doctoral level psychologist. To ensure reliable diagnostic procedures, our consultant, Dr. Barbara Rothbaum, trained all psychologists in formalized CAPS assessment procedures. Additional participant inclusion criteria included: (a) history of deployment in support of OIF/OEF, and (b) a non-sexual assault, deployment-related trauma that met criteria for PTSD according to the CAPS. Participants also had to agree not to initiate other psychotherapy for PTSD or new psychotropic medications.

After returning home from a deployment, Soldiers commonly experience a period of psychological readjustment during which most return to baseline functioning without treatment. To ensure that any treatment effects observed in the proposed study were not due to the normal recovery process, we excluded Soldiers who experienced a trauma within the previous 3 months. Additional exclusion criteria included: (a) a history of schizophrenia, bipolar, or other psychotic disorder, (b) a history of organic brain disorder, (c) current suicidal risk or self-mutilating behavior, as indicated by hospitalization in the past 6-months for risk of self-harm (d) an ongoing threatening situation (e.g. domestic violence), (e) current drug or alcohol dependence, (f) a history of seizures (a risk factor for VR adverse events), (g) prior history of PE therapy for PTSD, (h) a physical condition that interfered with the proper use of the Virtual Reality head mounted display or its peripherals, or (i) a loss of consciousness for a duration of greater than 15 minutes since entering active duty military service. Participants must have been stable on medications for at least 30 days.

Recruitment

Participants were recruited from the Behavioral Health Service at Womack Army Medical Center at Ft Bragg, NC.

During year one, the study team obtained IRB approval to conduct a clinical trial using human subjects. The protocol was approved as a multi-site study with Madigan Army Medical Center (MAMC) as the IRB of record with Womack Army Medical Center (WAMC) IRB deferring oversight to MAMC. Advertisements and consent forms were approved. Study staff were hired and training provided for the Multi-site Research Director, local site manager, and 2 clinical psychologists.

During year two, the study team completed hiring, credentialing and protocol training of the clinical psychologists in the outcomes assessor and treating clinician roles. Initial recruitment for this study began in July 2011. During year two, 46 referrals for treatment were received. Thirteen subjects consented to study participation and 4 of those met all of the inclusion and none of the exclusion criteria and were randomized to treatment. Of the 2 subjects randomized to the waitlist condition, 1 completed study participation through the post-assessment and 1 withdrew consent. Of the 2 subjects randomized to either active treatment group, 1 was dropped by the study team due to termination of the treating psychologist (see challenges below) and the other withdrew consent prior to completing the treatment phase.

During year three, the study team recruited, hired, credentialed and completed protocol training with a new clinical psychologist to replace the previously terminated treatment psychologist. After training of the new psychologist was completed, the study re-launched recruitment in June of 2013. During year three, a total of 91 new referrals were received and 41 subjects consented to study participation. Fifteen subjects met inclusion and exclusion criteria and were randomized.

At the conclusion of the study, a total of 175 soldiers were referred, 79 consented, 23 soldiers were randomized, 56 screen failed. Of the 23 randomized subjects, 9 completed all study related assessments and 4 were excluded as outlined above. Ten subjects withdrew prior to completing all study assessments, 4 of which had completed the treatment phase and withdrew during the follow-up phase of the study.

Study data from the original site/grant (for which this site was intended to be an extension) were analyzed and the results indicated that at posttreatment and follow-up, VR was less efficacious in reducing CAPS scores than was PE. This information was relayed to the MAMC IRB (IRB of record) and further analysis was requested by both MRMC and MAMC IRB. As a result of these data analyses, it was determined that recruitment would cease, and all currently enrolled subjects would complete follow-ups as scheduled.

Prolonged Exposure Therapy Protocol

Prolonged Exposure therapy consisted of 10 treatment sessions (lasting 90-120 minutes each), delivered weekly or twice-weekly, although flexibility was allowed to accommodate Soldier's training schedules. The formal protocol for prolonged exposure was followed. In the initial two sessions, the patient and therapist discussed the treatment rationale, talked about the client's reactions to trauma, and collaboratively developed a hierarchy of anxiety-provoking situations for in vivo exposure homework assignments. Session 3 marked the first imaginal exposure session and subsequent discussion of the exposure experience. Sessions 4-9 focused on prolonged imaginal exposure during which Soldiers revisted the trauma in as much detail as possible in the present tense, with subsequent discussions of their thoughts and feelings. Subjective Units of Distress scale were gathered every 5 minutes during imaginal exposure. Homework assignments following sessions 3-9 included listening to taped imaginal exposure sessions and in vivo exposure assignments. The final session included a final imaginal exposure, discussion of in vivo exposure, and a treatment progress review. The final part of the session focused on follow-up assessments and the termination of treatment.

Virtual Reality Exposure Therapy Protocol

The VRET protocol followed the same procedures as the PE protocol with the primary exception that all instances of imaginal exposure were augmented by immersion into *Virtual Iraq* environments. Similar to procedures for imaginal exposure, Soldiers revisited their trauma, telling it in the first person, present tense while the therapist customized Virtual Iraq to resemble events described. Two *Virtual Iraq* environments were utilized, specifically a city and a convoy environment. The two environments provided the clinician with flexibility to determine which environment best matched the patient's needs, based on her or his combat-related experiences. Both environments could be adjusted to match time of day (dawn, day, dusk, night), weather condition (sunny or sandstorm), and relational viewpoint (e.g., driver or passenger seat) to best reconstruct the patients traumatic experience. As soldiers navigated through these environments, the clinician could activate different audio (i.e., incoming mortars, weapons fire, voices, wind, etc.) and audiovisual stimuli (e.g., helicopter flyovers) to further approximate the traumatic experience.

Protocol Adherence

All therapy sessions were video recorded and 15% of planned sessions were randomly selected in advance for independent rating of treatment adherence and competence. Therapists were unaware of which sessions would be sent out for adherence review. Coders were not involved in other aspects of the study and were selected for this role based on experience as investigators on previous clinical trials of PE (Mary Heekin) and VRE (Judith Cukor). Treatment adherence forms used in previous clinical trials of PE (Barbara Olasov Rothbaum, Astin, &

Marsteller, 2005) were used for PE and adapted for VRE. Videos were coded, reviewed, and feedback provided to therapists on an on-going basis throughout the trial for fidelity review and adherence monitoring (Barber, Triffleman, & Marmar, 2007).

Outcome Measures

Screening

The following measures were administered prior to randomization to ensure eligibility and capture baseline data.

Clinical and Stigma Outcomes

The following clinical and stigma outcome measures were administered at baseline, and after 5 and I0 treatment sessions. The CAPS, PCL, IASMHS, and stigma measures were also assessed at 12 and 24-weeks following treatment.

I) *Clinician-Administered PTSD Scale (CAPS)* (1). The CAPS is a structured interview that assesses all DSM-IV PTSD criteria in terms of frequency and intensity. Scores are computed for Intrusion, Avoidance, and Hyperarousal symptom clusters, as well a Total score. The CAPS is commonly used as a primary outcome measure in PTSD clinical trials (2). The CAPS Current and Lifetime Version, which measures a one month symptom-duration, was used for the Baseline and Follow-up assessments. The CAPS One Week Version, which measures a one week symptom duration, was used to assess participants at baseline and after Treatment Sessions 5 and 10. PTSD severity as measured by CAPS served as the primary PTSD outcome in this study.

2) *PTSD Checklist (PCL)* (3). The PCL is a self-report measure that evaluates all 17 PTSD criteria using a 5-point Likert scale. Sensitivity and specificity are reportedly .82 and .83, respectively for detecting DSM PTSD diagnoses.

3) *Beck Depression Inventory-II (BDI-II)* (4). This self-report measure of depression contains 21-items that are rated on a 4-point scale.

4) *Beck Anxiety Inventory (BAI)* (5). The BAI is a self-report measure consisting of 21 items designed to discriminate anxiety from depression. It has high internal consistency (.92) and I-week test-retest reliability (.75) and discriminates anxious from nonanxious diagnostic groups.

5) *Inventory of Attitudes Toward Seeking Mental Health Services (IASMHS)* (6-7). The IASMHS is a 24 item assessment of help-seeking attitudes. It includes the following three factors based on components of Ajzen's Theory of Plarmed Behavior (8): Psychological Openness, Help-seeking Propensity, and Indifference to Stigma. Alpha coefficients for the subscales range from. 79 to .82, and internal consistency for the full inventory is .87. Test-retest reliability for the factors ranges from moderate to high. Convergent validity is demonstrated by effectively differentiating those who would and would not use services.

6) *Perceived Stigma Measures.* Stigma was measured using two 5-question assessment scales. 1) The 5-Item Perceived Stigma Scale was adapted from a scale developed by Komiya (9), and later adapted for use in a study of veterans by Pyne et al who found that depression severity scores were associated with higher levels of perceived stigma. Komiya (9) reported a coeffieient alpha of 0.72. As with the Pyne study, questions were adapted to receiving help for PTSD. 2) The second measure is a scale adapted from an inventory concerning stigmatization associated with completing psychological assessments (10) (5).

In-Session Assessments
The following assessments were used to determine levels of emotional and physiological engagement during treatment sessions.

1) *Subjective Units of Distress (SUDs)* (11).Ranging from 1 to 100, Subjective Units of Distress were gathered every 5 minutes during imaginal exposure to determine levels of distress and engagement in the situation.

2) *Physiological Data.* Heart rate, skin conductance, respirations, and peripheral skin temperature data were collected with the Biopac MPl50 (Biopac Systems, Inc.). The final analyses of these data have not yet been completed and will not be summarized below.

Patient Satisfaction Measure
The Client Satisfaction Questionnaire (CSQ) is an 18-item self-report measure of general satisfaction with treatment. Participants were asked to rate variables on a 4-point scale including the kind of service, treatment staff, quality of service, amount, length and quantity of service, outcome of service, general satisfaction, and procedures. Internal consistency and construct validity have been established (12) and the measure is widely used in research.

Challenges
A summary of challenges throughout this project has been compiled for this report.

Year 1: As previously reported, during the first year recruitment of appropriate candidates for the 2 clinical psychologist positions was a challenge due to the requirements of the military facility for credentialing, the limited availability of qualified candidates, and likely, the desirability of the geographic location of the duty location.

Year 2: During the second year, study enrollment was further delayed by the termination of the treating clinical psychologist for inability to meet supervisor criteria for appropriate treatment delivery consistent with the protocol. The hiring, credentialing and training of the new psychologist was completed during quarter 2 of year 3, and recruitment for the study was able to recommence during quarter 3.

During quarter 3, Year 2, the WAMC site clinical research coordinator relocated and resigned her position. The study team was able to relocate the part-time study project manager (previously located at MAMC) to WAMC and hire a part-time research assistant to fill the role of site CRC.

Finally, the results of the data analysis from the original grant that funded the recruitment at Joint Base Lewis-McChord resulted in the early termination of this study.

KEY RESEARCH ACCOMPLISHMENTS:

- This study added a recruitment site to one of the first randomized trials of PE with active duty military personnel and the first clinical trial comparing VRET to a standard of care.
- Transparently reported methods and findings will make important contributions to our understanding of how to care for Warriors with deployment related PTSD.

REPORTABLE OUTCOMES:

An extensive description of the outcomes are available in the final report for Award Number W81XWH-08-2-0015: Comparing Virtual Reality Exposure Therapy to Prolonged Exposure in the Treatment of Soldiers with PTSD, which is the original study award referenced throughout this report and for which this study was intended to be an extension.

Extensive communications with the IRB, the funding agency, the Science Officer, and others at CDMRP occurred during the end of year 4. The intent of these discussions was to ensure all statistical analyses were handled appropriately, outcomes were reported accurately and processes related to the handling of the study sites and data were appropriate. The results of the original study are available and will be published in peer reviewed publications.

CONCLUSION:

The study for which this was an intended extension represents the first assessor blinded, randomized study of PE with active duty military members in addition to being the first randomized, controlled trial comparing PE and VRET. As such, its findings documenting the efficacy of these treatments represent a significant contribution to our understanding of effective treatments for PTSD. In addition, the study demonstrated that PE without VR was superior to PE with VR (VRET). This finding was in contrast to the hypothesized outcome that VRET would be superior to PE alone. While multiple potential explanations for this finding exist, including the potential for VR to be effective with some subgroups of patients, the finding will inform future research as well as the current care of active duty soldiers with PTSD.

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APPENDICES:

None